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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/590,375	06/09/2000	Keiji Endo	2173-0120P	2206

7590 06/16/2004

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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/590,375	ENDO ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-10,12,13,15 and 17-29* is/are pending in the application.

4a) Of the above claim(s) *7-9* is/are withdrawn from consideration.

5)☒ Claim(s) *25-27* is/are allowed.

6)☒ Claim(s) *1,3,5,6,10,12,13,15,17-24, 28, 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 22, 2004 has been entered.

The AF amendment field January 21, 2004 canceling claims 14 and 16, amending claims 1, 3, 5, 6, 12, 13 and 17-24 and adding claims 28-29 has been entered.

Claims 1, 3, 5-10, 12, 13, 15 and 17-29 are pending. Claims 7-9 are withdrawn (see Office action mailed February 25, 2003). Claims 1, 3, 5, 6, 10, 12, 13, 15 and 17-29 are under consideration.

Claim Objections

Claim 13 is objected to because of the following informalities: the claim recites "alkaline conditions". The term "alkaline pH region", for example, is suggested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 10, 12, 13, 15, 17-24, 28 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 10, 12, 13, 15, 17-24 and 28 recite a mutant α-amylase comprising an amino acid sequence which is at least 95% homologous to SEQ ID NO:1. Claim 29 recites a mutant α-amylase comprising an amino acid sequence which is at least 95% homologous to SEQ ID NO:4. While the specification teaches that SEQ ID NO:4 of the instant invention is at least 95% homologous to SEQ ID NO: 1 of the instant invention (page 5, lines 19-27), the examiner is unable to locate adequate support in the specification for a genus of mutant α-amylases having 95% homology to SEQ ID NO:1 or SEQ ID NO:4. Thus, there is no indication that mutant α-amylases having an amino acid sequence which is at least 95% homologous to SEQ ID NO:1 were within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claims 1, 3, 5, 6, 10, 12, 13, 15 and 17-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mutant α-amylase

obtained by a specific disclosed substitution at a single position selected from the group consisting of positions 11, 16, 49, 84, 144, 167, 169, 178, 188, 190, 205 and 209 in SEQ ID NO:1, specific multiple mutants mutated at positions 167/169, 190/209, 144/190/209, 16/144/190/209, 167/169/190/209, 107/167/169/190/209, 49/107/167/169/190/209, 49/107/205/167/169/190/209 of SEQ ID NO:1, wherein said mutant α-amylase has an increased heat resistance and maintain resistance to chelating agents and high specific activity when compared to SEQ ID NO: 1, does not reasonably provide enablement for a mutant α-amylase obtained from a parent α-amylase having at least 70% homology to SEQ ID NO:1 with said mutations, wherein said mutant α-amylase has increased heat resistance and maintains resistance to chelating agents and high specific activity when compared to SEQ ID NO:1 and at least 95% or no known homology to SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1, 10, 12, 13, 15 and 17-24 are so broad as to encompass any mutant α-amylase of a parent α-amylase having at least 70% homology to SEQ ID NO:1 in which the amino acid corresponding to the specific positions in SEQ ID NO: 1 are mutated, said mutant α-amylase having increased heat resistance and maintaining resistance to chelating agents and optionally high specific activity and an amino acid sequence that is at least 95% homologous to SEQ ID NO:1. Claims 3, 5, 6 are so broad as to encompass any mutant α-amylase of a parent α-amylase having at least 70% homology to SEQ ID NO:1 in which the amino acid corresponding to the specific positions in SEQ

ID NO: 1 are mutated, said mutant α-amylase having increased heat resistance and maintaining resistance to chelating agents and an amino acid sequence with no known homology to SEQ ID NO:1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of mutant α-amylases broadly encompassed by the claims.

In order to make a mutant α-amylase with the requisite properties from a parent α-amylase having an amino acid sequence at least 70% homologous to SEQ ID NO:1 and having no requisite properties, one of ordinary skill in the art must transform said parent 70% homologous sequence to the sequence with the properties of SEQ ID NO:1. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the mutants of a single α-amylase having the amino acid sequence of SEQ ID NO:1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is

unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass mutant α-amylases with at least 95% or no known homology to SEQ ID NO:1 obtained from parent α-amylases with at least 70% homology to SEQ ID NO:1 in which the amino acid corresponding to specific residues recited in the claims are mutated because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting α-amylase activity; (B) the general tolerance of amylases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any α-amylase residues with an expectation of obtaining any α-amylase activity or α-amylase activity combined with increased heat resistance and resistance to chelating agents and high specific activity; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

With regard to claims 1 and 13, the specification provides neither guidance, rational nor predictable scheme for modifying any α-amylase residues with an expectation of obtaining α-amylase activity combined with increased heat resistance and resistance to chelating agents or α-amylase activity combined with increased heat resistance and resistance to chelating agents and high specific activity. Thus, the specification does not identify residues that are responsible for heat resistance, resistance to chelating agents or specific activity in α-amylase of SEQ ID NO:1.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including amino acid modifications in a parent α-amylase having no requisite properties and having an amino acid sequence at least 70% homologous to SEQ ID NO:1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, making a mutant α-amylase from a parent α-amylase having 70% homology to SEQ ID NO:1 and comprising a specific mutation and having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 13, 15, 17-24 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is unclear as not indicating at which positions mutations are made in a sequence that is 70% homologous to SEQ ID NO:1. Amending the claim to recite positions in sequence that is 70% homologous to SEQ ID NO:1 corresponding to the specific (recited) positions in SEQ ID NO:1, for example, (similarly to claim 1) would obviate this rejection.

Claim 13, with dependent claims 15, 17-24, recites "(ii) maintains resistance to chelating agents when compared to SEQ ID NO:1" while "(iii) maintains high specific activity under alkaline conditions". "high" is a relative term, the metes and bounds of which are unascertainable without comparison to SEQ ID NO:1.

Claim 29 is confusing as drawn to a mutant of SEQ ID NO:4 that is compared in its properties to SEQ ID NO:1.

Allowable Subject Matter

Claims 25-27 are allowed.

Response to Arguments

Applicant's arguments filed January 21, 2004 have been fully considered but they are not persuasive.

With regard to the new matter rejection of a mutant α-amylase having an amino acid sequence at least 95% homologous to SEQ ID NO:1, "Applicants respectfully disagree with the Examiner on this point. In the Reply filed on July 25, 2003, Applicants pointed out several examples of final mutant α-amylase sequences having at least 95% homology to SEQ ID NO:1 (see, the table on page 13 of the Reply). The Examiner does not seem to respond to these arguments in the outstanding Office Action. Therefore, the Examiner is requested to withdraw this rejection" (Remarks, page 15). This is not persuasive because while Applicants pointed out several specific mutant α-amylase sequences each of which having at least 95% homology to SEQ ID NO:1 , the claims are not drawn to said specific mutant α-amylase sequences but to a genus of mutant α-

amylase sequences having 95% homology to SEQ ID NO:1. Support for the specific species that are not claimed does not translate to the support for the claimed genus. The property of being 95% homologous to SEQ ID NO: 1, said property common to all species within a genus is not supported by the specification.

With regard to the enablement, "Applicants respectfully traverse the rejection applied to the pending claims and withdrawal of the instant rejection are respectfully requested. The Examiner asserts that final mutant sequences having 70% homology to SEQ ID NO:1 are not enabled by the specification. Claims 1 and 13 are amended to recite that the final mutant sequences have 95% homology to SEQ ID NO:1" (pages 17-18). This is not persuasive because to obtain said mutant with 95% homology to SEQ ID NO;1 one of ordinary skill in the art should start with an α-amylase that has no requisite properties and a sequence that is only 70% homologous to SEQ ID NO:1. Applicants continue "With regard to the homology of the final mutant sequence, the skilled artisan can readily ascertain that if the parent sequence has 70% homology to SEQ ID NO: 1, then only substitutions/deletions can be made that actually increase or maintain the homology of the final mutant sequence at 95%" (paragraph bridging pages 18-19). This is not persuasive because there is no guidance in the specification as to where said substitutions/deletions can be made to impart the requisite properties to the parent α-amylase having no such properties.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

June 10, 2004